

CLAIMS

1. An antibody which catalyzes hydrolysis of  $\beta$ -amyloid at a predetermined amide linkage.
2. The antibody of Claim 1 which catalyzes hydrolysis of the amide linkage between residues 39 and 40 of  $\beta$ -amyloid.
3. The antibody of Claim 1 which catalyzes hydrolysis of the amide linkage between residues 40 and 41 of  $\beta$ -amyloid.
4. The antibody of Claim 1 which catalyzes hydrolysis of the amide linkage between residues 41 and 42 of  $\beta$ -amyloid.
5. The antibody of Claim 1 which preferentially binds a transition state analog which mimics the transition state adopted by  $\beta$ -amyloid during hydrolysis at a predetermined amide linkage, and also binds to natural  $\beta$ -amyloid with sufficient affinity to detect using an ELISA.
6. The antibody of Claim 1 which preferentially binds a transition state analog which mimics the transition state adopted by  $\beta$ -amyloid during hydrolysis at a predetermined amide linkage, and does not bind natural  $\beta$ -amyloid with sufficient affinity to detect using an ELISA.

7. A vectorized antibody which is characterized by the ability to cross the blood brain barrier and the ability to catalyze the hydrolysis of  $\beta$ -amyloid at a predetermined amide linkage.
8. The vectorized antibody of Claim 7 which is a bispecific antibody.
9. The vectorized antibody of Claim 8 which has a first specificity for the transferrin receptor and a second specificity for a transition state adopted by  $\beta$ -amyloid during hydrolysis.
10. The vectorized antibody of Claim 9 which catalyzes hydrolysis of  $\beta$ -amyloid between residues 39 and 40.
11. A method for sequestering free  $\beta$ -amyloid in the bloodstream of an animal, comprising the steps:
  - a) providing antibodies specific for  $\beta$ -amyloid; and
  - b) intravenously administering the antibodies to the animal in an amount sufficient to increase retention of  $\beta$ -amyloid in the circulation.
12. A method for sequestering free  $\beta$ -amyloid in the bloodstream of an animal, comprising the steps:
  - a) providing an antigen comprised of an epitope which is present on endogenous  $\beta$ -amyloid; and
  - b) immunizing the animal with the antigen of step a) under conditions appropriate for the generation of antibodies which bind endogenous  $\beta$ -amyloid.
13. A method for reducing levels of  $\beta$ -amyloid in the brain of an animal, comprising the steps:

- a) providing antibodies specific for  $\beta$ -amyloid endogenous to the animal; and
  - b) intravenously administering the antibodies to the animal in an amount sufficient to increase retention of  $\beta$ -amyloid in the circulation of the animal.
14. The method of Claim 13 wherein the antibodies specific for  $\beta$ -amyloid are catalytic antibodies which catalyze hydrolysis of  $\beta$ -amyloid at a predetermined amide linkage.
15. The method of Claim 13 wherein the antibodies are monoclonal.
16. The method of Claim 13 wherein the antibodies are polyclonal.
17. The method of Claim 13 wherein the antibodies specifically recognize epitopes on the C-terminus of  $\beta$ -amyloid<sub>1-43</sub>.
18. A method for reducing levels of  $\beta$ -amyloid in the brain of an animal, comprising the steps:
- a) providing an antigen comprised of an epitope which is present on  $\beta$ -amyloid endogenous to the animal; and
  - b) immunizing the animal with the antigen of step a) under conditions appropriate for the generation of antibodies which bind endogenous  $\beta$ -amyloid.

19. The method of Claim 18 wherein the antigen is a transition state analog which mimics the transition state adopted by  $\beta$ -amyloid during hydrolysis at a predetermined amide linkage.
20. The method of Claim 18 wherein the antigen is comprised of  $A\beta_{10-25}$ .
21. The method of Claim 19 wherein the antibodies generated have a higher affinity for the transition state analog than for natural  $\beta$ -amyloid.
22. The method of Claim 19 wherein the antibodies generated catalyze hydrolysis of endogenous  $\beta$ -amyloid.
23. A method for preventing the formation of amyloid plaques in the brain of an animal, comprising the steps:
  - a) providing an antigen comprised of an epitope which is present on  $\beta$ -amyloid endogenous to the animal; and
  - b) immunizing the animal with the antigen of step a) under conditions appropriate for the generation of antibodies which bind endogenous  $\beta$ -amyloid.
24. The method of Claim 23 wherein the antigen is a transition state analog which mimics the transition state adopted by  $\beta$ -amyloid during hydrolysis at a predetermined amide linkage.
25. A method for reducing levels of circulating  $\beta$ -amyloid in an animal, comprising the steps:

- a) providing an antigen comprised of an epitope which is a mimic of a predetermined hydrolysis transition state of a  $\beta$ -amyloid polypeptide endogenous to the animal; and
  - b) immunizing the animal with the antigen of step a) under conditions appropriate for the generation of antibodies to the  $\beta$ -amyloid hydrolysis transition state.
26. A method for reducing levels of circulating  $\beta$ -amyloid in an animal, comprising the steps:
- a) providing antibodies which catalyze the hydrolysis of  $\beta$ -amyloid endogenous to the animal; and
  - b) intravenously administering the antibodies to the animal.
27. A method for preventing the formation of amyloid plaques in the brain of an animal, comprising the steps:
- a) providing antibodies which catalyze hydrolysis of  $\beta$ -amyloid produced by the animal at a predetermined amide linkage; and
  - b) administering the antibodies to the animal in an amount sufficient to cause a significant reduction in  $\beta$ -amyloid levels in the blood of the animal.
28. A method for reducing levels of  $\beta$ -amyloid in the brain of an animal, comprising the steps:
- a) providing vectorized bispecific antibodies competent to transcytose across the blood brain barrier, which catalyze hydrolysis of  $\beta$ -amyloid of the animal at a predetermined amide linkage; and
  - b) intravenously administering the antibodies to the animal.

29. The method of Claim 28 wherein the vectorized bispecific antibodies specifically bind the transferrin receptor.
30. The method of Claim 28 wherein the vectorized bispecific antibodies catalyze hydrolysis of the amide linkage between residues 39 and 40 of  $\beta$ -amyloid.
31. A method for disaggregating amyloid plaques present in the brain of an animal comprising the steps:
  - a) providing vectorized bispecific antibodies competent to transcytose across the blood brain barrier, which catalyze hydrolysis of  $\beta$ -amyloid produced by the animal at a predetermined amide linkage; and
  - b) intravenously administering the antibodies to the animal in an amount sufficient to cause significant reduction in  $\beta$ -amyloid levels in the brain of the animal.
32. A method for disaggregating amyloid plaques present in the brain of an animal, comprising the steps:
  - a) providing antibodies which catalyze hydrolysis of  $\beta$ -amyloid produced by the animal at a predetermined amide linkage; and
  - b) administering the antibodies to the animal.
33. A method for generating antibodies which catalyze hydrolysis of a protein or polypeptide comprising the steps:
  - a) providing an antigen, the antigen being comprised of an epitope which has a statine analog which mimics the conformation of a predetermined hydrolysis transition state of the polypeptide;

- b) immunizing an animal with the antigen under conditions appropriate for the generation of antibodies to the hydrolysis transition state.
34. The method of Claim 33 wherein the protein is  $\beta$ -amyloid.
35. A method for generating antibodies which catalyze hydrolysis of a protein or polypeptide comprising the steps:
- a) providing an antigen, the antigen being comprised of an epitope which has a reduced peptide bond analog which mimics the conformation of a predetermined hydrolysis transition state of the polypeptide;
  - b) immunizing an animal with the antigen under conditions appropriate for the generation of antibodies to the hydrolysis transition state.
36. The method of Claim 35 wherein the protein is  $\beta$ -amyloid.